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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/586,242	06/02/00	MCKIM J	28341/6281A

EXAMINER	
OZGA, B	
ART UNIT	**PAPER NUMBER**
1651	6

HM12/0328

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DATE MAILED: 03/28/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/586,242	MCKIM ET AL.	
	Examiner	Art Unit	
	Brett T Ozga	1651	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-42 is/are pending in the application.

4a) Of the above claim(s) 39-42 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-38 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims 1-42 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-38, drawn to methods of determining cytotoxicity, classified in class 435, subclass 29.

II. Claims 39-42, drawn to kits for determining cytotoxicity, classified in class 435, subclass 29.

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, determining cytotoxicity could be accomplished with determination of other organelle functioning, not just mitochondrial.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their recognized divergent subject matter placing an undue burden to search divergent subjects in the non- patent literature, restriction for examination purposes as indicated is proper.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement may be traversed (37 CFR 1.143).

During a telephone conversation with Nabeela McMillan on 1/18/01, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-38. Affirmation of this election must be made by applicant in responding to this Office Action. Claims 39-42 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kangas et al. (Med Biol, 62:338-343, 1984) in view of Redick et al. (J. Biol. Chem, 257:15200-3) and Connors et al. (Biochem Pharmacol 24:2217-24, 1975).

The instant application's first independent claim is a method of predicting the in vivo cytotoxicity of a chemical compound comprising: culturing cells in a culture medium that comprises a plurality of concentrations of said chemical compound; measuring three indicators of cell health; and predicting a toxic concentration of said chemical

compound from the measurements. Dependent claims further limit by choosing the indicators from those for cellular replication, membrane integrity, mortality, mitochondrial function, and intracellular energy balance. They also limit by using a concentration range from 0-300 micromolar.

Dependent claims further limit by monitoring cellular replication with an assay that measures H-thymindine incorporation and mitochondrial function with an ATP assay. They further limit by choosing the cells from liver cell lines and being used to treat cancer.

Kangas and Redick teach ATP assays, MTT assays, Alamar Blue assays and Rhodamine 123 assays, all of which are well known in the art.

Kangas et al. teach a method of predicting the cytotoxicity of a chemical compound comprising: culturing cells in a culture medium (see abstract) and measuring cell mortality, cellular replication, mitochondrial function with an ATP assay and intracellular energy balance. (See paragraph 1 of introduction) Kangas et al. also teach the treatment of cancer (see abstract). Kangas does not teach in vivo or choosing the cells from liver cells lines.

Redick teaches choosing the cells to be used in predicting the cytotoxicity of chemical compounds from liver cell lines (See methods) and Connors et al. teach in vivo methods of screening for anti-cancer agents and predicting the cytotoxicity of chemical compounds. (See "anti-tumour selectivity" section)

One of ordinary skill in the art would been motivated to modify the teaching of Kangas et al. by the addition of liver cell lines as taught by Redick and in vivo as taught

by Connors based on the common cytotoxic agents (i. e. antitumor agents) found in each of the references

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the teaching of Kangas et al. by the addition of liver cell lines as taught by Redick and in vivo as taught by Connors to attain the advantages of such as disclosed by Connors, namely to facilitate the use of the techniques in real world pharmaceutical compositions instead of merely in vitro testing.

, Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brett T Ozga whose telephone number is 7033050634. The examiner can normally be reached on M-F 0530-1500, 2nd Wednesday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 7033084743. The fax phone numbers for the organization where this application or proceeding is assigned are 7033084242 for regular communications and 7033053014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 7033080196.

BTO
March 21, 2001

JEAN C. WITZ
PRIMARY EXAMINER